AGRANULOCYTOSIS DURING MULTIDRUG THERAPY (MDT) OF LEPROSY

Sir,

Agranulocytosis is a recognized side-effect of dapsone but until recently had not been reported during leprosy treatment.[1] In 1986 the first case of agranulocytosis complicating the treatment of leprosy was reported in a Melanesian from Papua New Guinea.[2] I would like to report another case of agranulocytosis during multidrug therapy (MDT), in a Melanesian from Vanuatu.

A 29-year-old woman with a family history of leprosy was seen in the Outpatient Department of the Vila Central Hospital with foot drop, sensory loss of the lower leg and nerve enlargement. Skin smears for acid-fast bacilli were negative. A diagnosis of paucibacillary leprosy was made and MDT, including 100 mg dapsone daily, was started.

After 5 weeks she was admitted to the same hospital, having developed a fever and rash. She was pyrexial with an axillary temperature of 39·4 C. Her sclera were yellow and she had a generalized erythematous rash. Her liver was enlarged and tender and she had a palpable spleen. The sulphone syndrome secondary to dapsone was diagnosed, leprosy treatment was stopped and treatment with prednisone 60 mg daily was started. Investigations on admission included a haemoglobin of 8·6 g/dl with a white blood count of 29,300/mm^3. Blood film examination was interpreted as showing a left shift with atypical lymphocytes. Serum bilirubin was 478 micromol/l (normal range < 17) with very high transaminases, and 3 days after admission her skin began to desquamate. She remained very sick for several days but gradually improved.

She developed a fever 11 days after admission, and a cough with purulent sputum. There were a few crackles audible at the right base but a chest radiograph showed clear lung fields. Amoxycillin

500 mg 3 times daily was commenced, and 3 days later, 2 weeks after being admitted, her condition rapidly deteriorated, she began to cough blood and her blood pressure fell to 60/40 mmHg. Intravenous fluids were started and cloxacillin, gentamicin and chloramphenicol given. A repeat chest radiograph showed right upper lobe consolidation. Her white blood cell count was only 700/mm, with no neutrophils visible. Unfortunately she did not respond to treatment and died a few hours later.

Although there have been several reports of agranulocytosis due to dapsone, nearly all of these have been in patients taking dapsone for a reason other than leprosy. The first case of agranulocytosis secondary to dapsone occurred in a patient being treated for dermatitis herpetiformis.[3] A total of 16 US soldiers serving in Vietnam developed agranulocytosis while taking 25 mg dapsone daily as malaria prophylaxis,[4] of whom 8 died. Agranulocytosis has also been reported with weekly Maloprim (100 mg dapsone, 12·5 mg pyrimethamine) prophylaxis.[5]

Serious reactions, numbering 103, with 11 deaths, were reported to the national registers of Sweden and the UK during 1965–1988,[6] and 7 deaths were attributed to agranulocytosis. The incidence of serious reactions appeared to increase with higher doses.

In the last 4 years in Vanuatu we have been seeing a high incidence of the dapsone syndrome during leprosy treatment with nearly a quarter of patients reacting to dapsone (P Reeve *et al.* unpublished data). This usually rare syndrome has been reported in 2 brothers in Papua New Guinea[7] and in an Aboriginal mother and son in Australia (J. C. Hargrave, personal communication). It is interesting that the only other case of agranulocytosis complicating leprosy treatment was reported in a Melanesian, and it is possible that there could be an increased susceptibility to dapsone reactions in Melanesians.

Because of the high incidence of reactions to dapsone all new leprosy patients in Vanuatu are being admitted to hospital for the first 2 months of treatment for close supervision.

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